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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/824,178	04/02/2001	Jean-Marc Roch	6024.US.C1	8572

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EXAMINER	
PAK, MICHAEL D	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 03/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/824,178	ROCH ET AL.	
	Examiner	Art Unit	
	Michael Pak	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,8-19,24-29 and 41-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5, 8-19, 24-29, 41-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I in Paper No. 11 is acknowledged. Claims 1-5, 8-19, 23-29, and 41-44 are pending.

2. Preliminary amendments filed 30 October 2002 (Paper No. 11) and 2 April 2001 (Paper No. 1.5). Claims 6, 7, 20-22 and 30-40 were cancelled in Paper No. 1.5).

Double Patenting

3. Claims 41-42 are objected to under 37 CFR 1.75 as being a substantial duplicate of claims 43-44. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-2 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is confusing and ambiguous because it is not clear what is the metes and bounds of the term "human endosulfine" because no structural limitation defines the metes and bounds of the molecule. The bovine and the human contain sequence fragments which are identical in many of the regions (see figure 3 of the specification). Thus, if the polynucleotide encodes an endosulfine which comprises the overlapping region it is not clear what determines the metes and bound of a human versus a bovine endosulfine or endosulfine from any other animal or cell.

Claim 1 is confusing and ambiguous because it is not clear what is the metes and bounds of the term "complement thereof" because complement is not a term used by one of skilled in the art. It is suggested that the claim limitation recite "fully complementary sequence thereof."

Claim 2 recites the limitation "said is" in line 1. There is insufficient antecedent basis for this limitation in the claim. In order to expedite prosecution the examiner has assumed the term should be "said polynucleotide."

Claims 11-13 recite "the vector portion of said expression vector" which is confusing because all of the expression is the vector portion.

5. Claims 1-5, 8-10, 14-19, and 23-24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for, an isolated polynucleotide encoding a human endosulfine, where the polynucleotide comprises SEQ ID NO:1 or 2, or positions 107-460 of SEQ ID NO:1, or positions 107-472 of SEQ ID NO:2; and polynucleotide comprising fully complementary sequence thereof; an isolated recombinant expression vector comprising the isolated polynucleotide above, and an isolated host cell transfected with the expression vector thereof; and a method of producing a polypeptide of claim 23 and 24 using the isolated host cells above; does not reasonably provide enablement for, an isolated polynucleotide comprising a nucleotide sequence which encodes a human endosulfine or a fragment of said isolated polynucleotide; an isolated recombinant expression vector comprising the isolated polynucleotide above, and an isolated host cell transfected with the expression vector thereof; and a method of producing a polypeptide of claim 23 and 24 using the isolated host cells above. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The determination of whether undue experimentation is needed is based on examining the factors summarized *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988).

Breadth of the claims. The claims encompass an isolated polynucleotide comprising a nucleotide sequence encoding variants and fragments of a human endosulfine, vectors comprising the nucleic acid thereof, and an isolated host cell

comprising the vector thereof, because the specification does not define human endosulfine and the specification on page 10, lines 23, define polynucleotide as nucleotides of any length including modifications and only refers to the primary structure of the molecule. Furthermore, the specification on page 10, lines 14, define polypeptide as a polypeptide with at least 3-5 amino acids. Thus the claims encompass a fragment of polynucleotide of 2 nucleic acids or a fragment of polypeptide of 3 amino acids. Furthermore, the claims encompass a variant polynucleotide because the term human endosulfine is not defined. The enablement rejection is directed mainly to how to use the polynucleotide and polypeptide fragment and variants of human endosulfine and the other claims encompass the polynucleotide and polypeptide variants and fragments of human endosulfine.

The nature of the invention. The nature of the invention is recombinant cloning of cDNA encoding human endosulfine and production of the endosulfine using host cells transfected with expression vectors comprising cDNA encoding human endosulfine. Invention also provides assays for endosulfine binding to sulfonylurea receptor where endosulfine is the natural ligand for the receptor.

The state of the prior art. The state of the prior art at the time of the invention was such that one skilled in the art has isolated nucleic acids encoding porcine endosulfine (Peyrollier et al.(Biochem. Biophys. Res. Comm., 1996). However, the specification does not teach how to use fragments and variants of the disclosed nucleic acid sequence which are 2 nucleic acids long. One of the uses for a polynucleotide fragment is for hybridization with other nucleic acid molecules. However, one skilled in

the art do not use polynucleotide fragments for hybridization that are smaller than 20 nucleotides (Wallace et al.(1987); page 434, second paragraph). Furthermore, a variant fragment is not always useful for hybridization for one skilled in the art. One skilled in the art do not use variant probes or random hybridization conditions to detect the desired specific nucleic acids because under non-optimal hybridization conditions the specific desired nucleic acid hybridization to the probe cannot be discriminated from the non-specific binding to undesirable nucleic acids. One skilled in the art calculates a number of parameters such as size, G-C content, self-complementarity, complexity, and hybridization conditions in relation to the specific goals to be achieved when using the particular hybridization method ((Wallace et al.(U); pages 434-439). Thus, hybridization is an unpredictable art and unless all the parameters for hybridization are considered, a fragment whose lengths are too short or a variant nucleic acid fragment is not sufficient to use for all nucleic acid hybridizations. Such fragments encompass a genus with a large number of species which are not reasonably expected to be functional.

One skilled in the art could utilize the fragment of nucleic acid sequence to encode a protein fragments. However, the specification does not teach how to use fragments and variants of the disclosed nucleic acid sequence which encode a fragment of polypeptide of 3 amino acids. Furthermore, one skilled in the art do not use a fragment of polypeptide less than 6 residues long to elicit antibodies (Harlow et al. (Antibodies, 1998, page 76, third paragraph). The lower limit of peptide length useful as antigen reflects the difficulty of recognizing the smaller peptides coupled to carriers (Harlow et al.(Antibodies, 1998) page 76, third paragraph). Furthermore, polypeptide

fragments and variants of 3 amino acids long would not be expected to encode a functional endosulfine with biological activity because the fragments would be out of frame with coding region and generally proteins require tertiary structural folding which is critical for biological activity which would be lacking such fragments (Bowie et al.(Science, 1987, page 1307, second column, second paragraph, last line). The experimentation necessary to use the nucleic acid variants and fragments for hybridization require empirical experimentation and thus is undue. The experimentation necessary to use the nucleic acid variants and fragments which encode a endosulfine also require empirical experimentation and thus is undue.

The quantity of experimentation necessary. The amount of experimentation required to use a fragment of polynucleotide which 2 nucleic acid long or encode a fragment of polypeptide 3 amino acid long is unpredictable because, as discussed above, the state of the art is unpredictable. The number of empirical experimentation necessary is unpredictable because the state of the art indicates the unpredictability of using a fragment of polynucleotide which 2 nucleic acid long or encode a fragment of polypeptide 3 amino acid long.

The predictability and unpredictability. The state of the art discussed immediately above indicate the unpredictability of using a fragment of polynucleotide which 2 nucleic acid long or encode a fragment of polypeptide 3 amino acid long and that one skilled in the art could not practice the claimed invention without empirically testing the various conditions which is undue.

The amount of direction of guidance provided. The specification provides guidance in making and using a polynucleotide encoding a human endosulfine where the polynucleotide comprises SEQ ID NO: 1 or 2 or the human endosulfine encodes. However, the specification fails to provide guidance to use a fragment of polynucleotide which 2 nucleic acid long or encode a fragment of polypeptide 3 amino acid long. One skilled in the art could not use such fragments without undue experimentation because of the state of the art is unpredictable for using such fragments.

The presence or absence of working examples of the invention. The specification provides working examples in making and using a polynucleotide encoding a human endosulfine where the polynucleotide comprises SEQ ID NO: 1 or 2 or the human endosulfine encodes. However, the specification fails to provide working examples of how to use a fragment of polynucleotide which 2 nucleic acid long or encode a fragment of polypeptide 3 amino acid long. One skilled in the art could not use such fragments without undue experimentation because of the state of the art is unpredictable for using such fragments.

In view of the extent and the unpredictability of the experimentation required to practice the invention as claimed, one skilled in the art could not make the invention without undue experimentation.

6. Claims 1, 8, 14, 15 and 23 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time

the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims encompass the generic receptors by name only but the essential feature of the invention is the endosulfine polypeptides of SEQ ID NO:2 and 4. The claims encompass a large genus of molecules whose structure and function is not claimed. However, the specification disclose the endosulfines of SEQ ID NO:2 and 4. *University of California v. Eli Lilly and Co. (CAFC) 43 USPQ2d 1398* held that a generic claim to human or mammalian when only the rat protein sequence was disclosed did not have written description in the specification. Thus, one of skilled in the art cannot envision the endosulfines which would have the essential feature of the invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application

filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

7. Claim 1, 8, 14, 15, 23 and 24 are rejected under 35 U.S.C. ' 102(b) as being anticipated by The United States of America (WO 93/16178).

The United States of America (USA) disclose EST1041 and EST1042 (pages 40-42) which have regions of 100% identity with SEQ ID NO:1 and 2 which meets the limitations of "human endosulfine" and "complements thereof." The nucleic acid of EST 1041 1-67 has only one mismatch at nucleic acid position 6 when compared to SEQ ID NO:1 nucleic acid position 390-456. USA teaches the expression vectors comprising the DNA sequences (page 88), the transfected and transformed cells with the expression vectors (page 88 and 90), and the expression and isolation of the expressed

protein (page 90). USA teach the isolation of complete cDNA and the determining of the reading frame, orientation, and coding regions(page 77).

Claim 1 encompass the nucleic acid of USA because of the claim limitation "human endosulfine" and "complements thereof" encompasses of the polynucleotide. The Examiner has interpreted the limitations of claims 2-5 Asaid nucleotide@ to be referring to the nucleotide sequence of claim 1. Since the limitation of Afragments@ in claim 1 is referring to the polynucleotide, claims 2-5 encompass the polynucleotide fragment due their dependence on claim 1.

8. Claim 1, 8, 14, 15, 23 and 24 are rejected under 35 U.S.C. ' 102(a) as being anticipated by Peyrollier et al.(Biochem. Biophys. Res. Comm., 1996).

Peyrollier et al. disclose the nucleic acid encoding a fragment of an endosulfine (page 585, Figure 2). Peyrollier et al. disclose the subclone of the nucleic acid encoding a fragment of an endosulfine in the expression plasmid pIBI31 and the transformants comprising the plasmid (page 584, second paragraph). The nucleic acid encoding an endosulfine fragment of Peyrollier et al. is 100% identical to SEQ ID NO:3 from residue 25-101. The term "human endosulfine" encompasses the endosulfine disclosed by Peyrollier et al. because there is no structural limitation in the claim.

9. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Hillier et al.(EMBL Database, 1996) is a cumulative reference with Peyrollier et al.(Biochem. Biophys. Res. Comm., 1996) because of the nucleic acid sequence fragment disclosed.

10. No claims are allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Pak whose telephone number is 703-305-7038. The examiner can normally be reached on Monday-Friday from 8:30 AM to 2:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for the organization where this application or proceeding is assigned is 703-308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

Michael D. Pak

Michael Pak
Primary Patent Examiner
Art Unit 1646
5 March 2003